PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Andrés RIVERA et al.

Application No.: 09/353,592

Filed: July 15, 1999

For: APPLICATOR FOR A POLYMERIZABLE MONOMER

Group Art Unit: 1772

Examiner: S. Hon

Docket No.: 101054

REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In reply to the September 3, 2003, Office Action, and the March 31, 2003, Decision on Appeal, and further to the Preliminary Amendment and Continued Prosecution Application filed on May 29, 2003, Applicants request reconsideration of the application in view of the following comments.

REMARKS

Claims 1-32 are pending herein.

Claims 1-32 are rejected under 35 U.S.C. §103(a) over Leung. The same rejection was made in the parent application with respect to then-pending claims 1-30, and was affirmed in the Decision on Appeal dated March 31, 2003. Applicants respectfully traverse the rejection based on the following new arguments and evidence.

Independent claim 1, representative of the claimed invention, is directed to an applicator for dispensing a polymerizable or cross-linkable material, comprising: an outer

container; an inner container disposed within said outer container, said inner container containing a polymerizable or cross-linkable material; and a rate modifier for said polymerizable or cross-linkable material disposed on an outer surface of said inner container. Leung would not have rendered obvious the claimed invention, because Leung fails to teach or suggest each and every limitation of the claimed invention. In particular, Leung fails to teach or suggest at least the limitation that a rate modifier for the polymerizable or cross-linkable material is disposed on an outer surface of said inner container.

A. Leung Does Not Teach or Suggest the Claimed Invention

Similar to the claimed invention, Leung is directed to an applicator for dispensing a synthetic or semi-synthetic polymerizable or cross-linkable monomer material. According to Leung, the applicator comprises an applicator tip comprising a solid support having a polymerization or cross-linking accelerator or initiator for the synthetic or semi-synthetic monomer material disposed thereon or therein, and a container body. The synthetic or semi-synthetic monomer material is located in the container body in a non-contacting relationship with the tip prior to dispensing the material. See Leung at Abstract and claim 1. For example, an embodiment of the disclosed applicator is shown in Leung Figure 3. According to Figure 3, the applicator of Leung includes an outer container 200 and an inner container 400 that contains an amount of monomer material 300 therein. According to this embodiment, the applicator tip 500 has the polymerization or cross-linking accelerator or initiator for the monomer material disposed therein or thereon. See also Leung at column 7, line 66 to column 8, line 4.

Leung also discloses several modification of the disclosed applicator. For example, Leung discloses that the polymerization or cross-linking accelerator or initiator can be located in the applicator at a position other than being loaded in or on the applicator tip. For example, at column 10, lines 43-53, Leung teaches that the accelerator or initiator may be

stored in a separate compartment within the outer container 200 separate form the polymerizable or cross-linkable monomer material. Alternatively, in the same passage, Leung discloses that "the applicator container may be lined or coated with the initiator ... for example, in the device of FIG. 3, the initiator may be coated on the internal surface of body 200."

Although Leung discloses these modifications of the disclosed applicator, Leung does not teach or suggest all of the limitations of the claimed invention. In particular, Leung at most discloses that the accelerator or initiator may be lined or coated on the internal surface of the outer container 200. However, this disclosure is entirely different from the limitation of independent claims 1 and 24 that the rate modifier for the polymerizable or cross-linkable material is disposed on an outer surface of the inner container. For example, with reference to Figure 1 of the present application, the rate modifier 50 according to the claimed invention is lined or coated on the outer surface of the inner container 40.

B. The Board of Appeals Affirmed the Rejection

In the Decision on Appeal, the Board affirmed the previous rejection. The Board held that, absent any evidence to the contrary, one of ordinary skill in the art would have been motivated to dispose the rate modifier for the polymerizable or cross-linkable material on an outer surface of the inner container, based on Leung's teachings that it can be disposed on the inner surface of the outer container. Applicants disagree with the Board's Decision, for all of the reasons set forth in Applicants' Appeal and Reply Briefs.

In the Decision, the Board stated that "Accordingly, one of ordinary skill in the art would have recognized that whether the rate modifier is initially coated on the inner surface of the outer container or the outer surface of the inner container, the resulting applicator would serve substantially the same function." Page 5, lines 13-17 (emphasis added). However, that statement was made in the Decision based on an unsupported assumption that

the relative location of the initiator would not result in different application properties. In fact, Applicants submit, for all of the reasons set forth below, that the location of the initiator does provided an unexpected benefit to the claimed invention. The evidence discussed below expressly disproves the unsupported assumption made in the Decision, and thereby evidences non-obviousness of the claimed invention.

C. Applicants Submit Evidence of Non-Obviousness

Even assuming that the Board's position and Decision were correct (albeit in the absence of any supporting evidence), which Applicants deny, any holding of obviousness can be rebutted by evidence of unexpected results. For example, as stated by the Federal Circuit in In re Wright, 848 F.2d 1216, 6 USPQ2d 1959 (Fed. Cir. 1988):

> Factors including unexpected results, new features, solution of a different problem, novel properties are all consideration in the determination of obviousness....

These secondary considerations (objective evidence of non-obviousness) must be evaluated before reaching an ultimate decision under 35 U.S.C. §103.

1. The Claimed Invention Provides Unexpected Results

In the present application, the attached Declaration demonstrates and establishes unexpected results of the claimed invention. In particular, the Declaration demonstrates that by disposing the rate modifier for the polymerizable or cross-linkable material on an outer surface of the inner container, as claimed, rather than in the applicator tip, as disclosed and preferred in Leung, a significant and unexpected result in terms of setting time and usefulness of the adhesive material is obtained.

The Declaration demonstrates a test in which two otherwise identical applicators were utilized, the difference being the location of the rate modifier for the polymerizable or cross-linkable material with respect to the monomer. In the experimental examples, the polymerizable or cross-linkable material was disposed on an outer surface of the inner

container according to the claimed invention. In the control experiments, the rate modifier for the polymerizable or cross-linkable material was disposed in the applicator tip, in the manner disclosed and preferred in Leung. Each of the applicators was then activated, and successive drops of adhesive were expressed through the applicator tips. The setting time of the adhesive drops was measured, as a means to determine how effective the placement of the rate modifier was to activate the polymerizable adhesive.

The experimental results demonstrate that for the preferred applicators of Leung (i.e., rate modifier for the polymerizable or cross-linkable material placed in the applicator tip), acceptable setting time was obtained for the first drop of adhesive, but initiation effectiveness quickly decreased, to the point that the applicator became ineffective. In contrast, the applicators prepared according to the present invention provided acceptable results for the first drop of adhesive, and improved results for subsequent drops. These results are unexpected benefits of the claimed invention, and are nowhere taught or suggested by Leung.

As a further comparison, the Declaration describes that an attempt was made to prepare similar samples, but where the rate modifier for the polymerizable or cross-linkable material is disposed on an inner surface of the outer container, as briefly mentioned as an option in Leung. However, such samples could not be prepared in a useable manner, as the solvents used to apply the rate modifier caused deformation of the butyrate tube.

2. The Declaration Results are Significant and Unexpected

The Declaration demonstrates that different placement of the polymerization initiator or rate modifier with respect to the monomer results in significant and unexpected differences in the polymerization process. That is, when the polymerization initiator or rate modifier is placed in the applicator tip, as in Leung, the first drop of expressed monomer contains a higher amount of initiator than successive drops, and eventually there is virtually no

polymerization initiator or rate modifier left in the applicator tip to be mixed with the monomer and thereby cause initiation or modification of the polymerization rate.

In contrast, when the polymerization initiator or rate modifier is placed on an outer surface of the inner container, as claimed, more uniform polymerization kinetics are observed. It is believed that by placing the polymerization initiator or rate modifier is placed on an outer surface of the inner container, as claimed, the polymerization initiator or rate modifier is more uniformly mixed with the monomer even prior to the monomer entering the applicator tip. Accordingly, the first drop of monomer expressed through the tip has substantially the same amount of initiator as successive drops of monomer expressed through the applicator tip.

The significance of this distinction is important during use of the claimed invention. In one exemplary embodiment of the invention, the claimed applicator, method of making an applicator, and method of applying a polymerizable or cross-linkable material to a substrate can be applied to the commercial DERMABOND® Topical Skin Adhesive product. A brochure describing that product, including exemplary methods of use, is attached hereto. As shown in the brochure, the polymerizable or cross-linkable material is used to seal such wounds as deep wounds, long lacerations, skin tears, non-linear wounds and facial lacerations. In such uses, it is important that consistent polymerization results be obtained for the full application amount of the polymerizable or cross-linkable material, so that proper wound closure can be obtained.

The attached Declaration thus establishes that, unexpectedly, the claimed invention provides more consistent results as compared to Leung. Such results are nowhere taught or suggested in Leung.

3. Conclusion

Accordingly, the attached Declaration demonstrates unexpected results of the claimed invention, supporting a conclusion of non-obviousness of the claimed invention.

D. Conclusion

For at least these reasons, the claimed invention would not have been obvious over Leung. Reconsideration and withdrawal of the rejection are respectfully requested.

Should the Examiner believe that anything further is necessary in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned Attorney at the telephone number listed below.

Respectfully submitted,

William P. Berridge
Registration No. 30,024

Joel S. Armstrong
Registration No. 36,430

WPB:JSA

Date: December 3, 2003

Attachment:
Declaration Under 37 C.F.R. §1.132
DERMABOND® Topical Skin Adhesive Brochure

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

Easy to Use...on a variety of wounds

For Millions of Adults and Children Treated for Lacerations in the ED[1]...

...Trust the DERMABOND® Family of Topical Skin Adhesives

Try high viscosity formula for better control

BEST AVAILABLE COPY

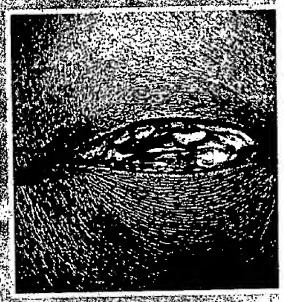
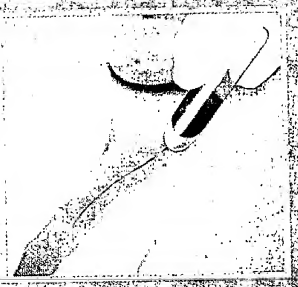
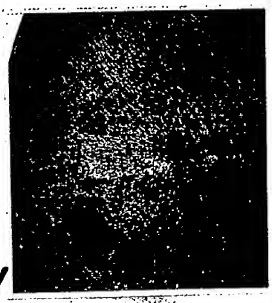
DERMABOND®
TOPICAL SKIN ADHESIVE
2-Octyl Cyanoacrylate

Advances in healing

Close a variety of easily approximated wounds—*and seal out bacteria that can lead to infection*

DERMABOND APPLICATION TECHNIQUE

1. Follow standard surgical practice for wound preparation and achieve hemostasis
2. Approximate skin edges and use deep dermal sutures to relieve tension if necessary
3. Crack the DERMABOND vial in the upright position, invert, and apply pressure to saturate the tip
4. Release pressure, then reapply pressure to express adhesive
5. Apply 3 thin layers of adhesive, waiting approximately 30 seconds between layers

	DEEP WOUND	LONG LACERATION
TRAUMATIC LACERATION		
LACERATION TECHNIQUE TIPS	 Deep wounds require deep sutures to relieve tension on skin edges prior to application of DERMABOND	 • Temporarily divide wound into segments using strips, forceps, or fingers • Approximate skin edges with DERMABOND • Don't put DERMABOND over the strip, as it will need to be removed
IMMEDIATE OUTCOME		

DERMABOND*

TOPICAL SKIN ADHESIVE
2-Octyl Cyanoacrylate

Advances in healing

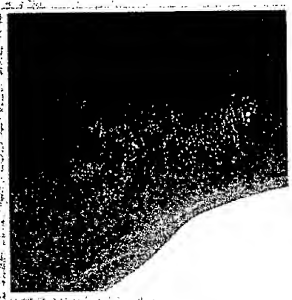
SKIN TEAR

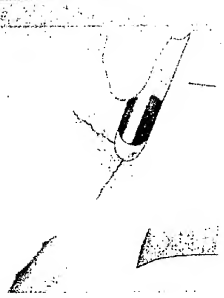
Bring skin edges together using a gauze pad

Apply DERMABOND in segments

Avoid getting DERMABOND under the skin tear

NON-LINEAR WOUND

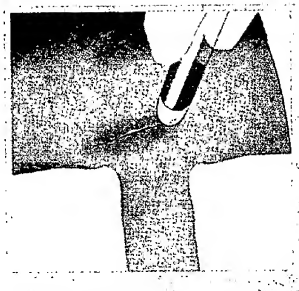




Ensure that all angles are aligned and approximated prior to application of DERMABOND

Apply DERMABOND in segments

FACIAL LACERATION



Position patient to avoid runoff into the eye area

Protect eye with petrolatum and a gauze pad

Get all the benefits of the leading topical skin adhesive...

Advantages of DERMABOND Adhesive

- Is easy to use
- Provides the strength of healed tissue at 7 days in less than 3 minutes[2]
- Is the first and only FDA-approved topical skin adhesive that protects wounds from bacteria that can cause infection
- Is more cost-effective than sutures[3-6]
- May relieve the anxiety of getting stitches
- Promotes a moist wound-healing environment
- Meets OSHA standards for needlestick safety

...Plus the choice of a new formulation

High Viscosity Formula That Is 6 Times Thicker[2]

- Minimizes runoff and provides better control

Applicator With Precision Tip Geometry

- Enables fine-line delivery of adhesive[2]
- Offers better delivery to hard-to-reach areas

Thicker Formula, Better Control

Original DERMABOND Adhesive With Dome and Chisel Tip Applicators

High Viscosity DERMABOND Adhesive With Dome and Precision Tip Applicators

DERMABOND*

TOPICAL SKIN ADHESIVE

2-Octyl Cyanoacrylate

Advances in healing

DERMABOND*

Topical Skin Adhesive
(2-Octyl Cyanoacrylate)

INDICATIONS
DERMABOND Topical Skin Adhesive is intended for topical application only to hold closed easily approximated skin edges of wounds from surgical incisions, including punctures from minimally invasive surgery, and simple, thoroughly cleansed, trauma-induced lacerations. DERMABOND adhesive may be used in conjunction with, but not in place of, deep dermal stitches.

CONTRAINDICATIONS
- Do not use on any wound with evidence of active infection, gangrene, or wounds of decubitus etiology.
- Do not use on mucosal surfaces or across mucocutaneous junctions (e.g., oral cavity, lips), or on skin which may be regularly exposed to body fluids or with dense natural hair, (e.g., scalp).
- Do not use on patients with a known hypersensitivity to cyanoacrylate or formaldehyde.

WARNINGS
- DERMABOND adhesive is a fast setting adhesive capable of adhering to most body tissue and many other materials, such as latex gloves and stainless steel. Inadvertent contact with any body tissue, and any surfaces or equipment that are not disposable or that cannot be readily cleaned with a solvent such as acetone should be avoided.
- Polymerization of DERMABOND adhesive may be accelerated by water or fluids containing alcohol: DERMABOND adhesive should not be applied to wet wounds.
- DERMABOND adhesive should not be applied to the eye. If contact with the eye occurs, flush the eye copiously with saline or water. If residual adhesive remains, apply topical ophthalmic ointment to help loosen the bond and contact an ophthalmologist.
- When closing facial wounds near the eye with DERMABOND adhesive, position the patient so that any run-off of adhesive is away from the eye. The eye should be closed and protected with gauze. Prophylactic placement of petroleum jelly around the eye, to act as a mechanical barrier or dam, can be effective in preventing inadvertent flow of adhesive into the eye. DERMABOND adhesive will not adhere to skin pre-coated with petroleum jelly. Therefore, avoid using petroleum jelly on any skin area where DERMABOND adhesive is intended to adhere. Use of DERMABOND adhesive near the eye has inadvertently caused some patient's eyelids to be sealed shut. In some of these cases, general anesthesia and surgical removal has been required to open the eyelid.
- DERMABOND adhesive should not be used below the skin because the polymerized material is not absorbed by tissue and can elicit a foreign body reaction.
- DERMABOND adhesive should not be used in high skin tension areas or across areas of increased skin tension, such as knuckles, elbows, or knees, unless the joint will be immobilized during the skin healing period.
- DERMABOND adhesive treated wounds should be monitored for signs of infection. Wounds with signs of infection, such as erythema, edema, warmth, pain and pus, should be evaluated and treated according to standard practice for infection.
- DERMABOND adhesive should not be used on wound sites that will be subjected to repeated or prolonged moisture or friction.
- DERMABOND adhesive should only be used after wounds have been cleaned and debrided in accordance with standard surgical practice. Local anesthetic should be used when necessary to assure adequate cleansing and debridement.
- Excessive pressure of the applicator tip against wound edges or surrounding skin can force the wound edges apart and allow adhesive into the wound. Adhesive within the wound could delay wound healing and/or result in adverse cosmetic outcome. Therefore, DERMABOND adhesive should be applied with a very light brushing motion of the applicator tip over easily approximated wound edges.
- DERMABOND adhesive polymerizes through an exothermic reaction in which a small amount of heat is released. With the proper technique of applying DERMABOND adhesive in multiple thin layers (at least three) onto a dry wound and allowing time for polymerization between applications, heat is released slowly and the sensation of heat or pain experienced by the patient is minimized. However, if DERMABOND adhesive is applied so that large droplets of liquid are allowed to remain unspread, the patient may experience a sensation of heat or discomfort.
- DERMABOND adhesive is packaged for single patient use. Discard remaining opened material after each wound closure procedure.
- Do not resterilize DERMABOND adhesive.
- Do not place DERMABOND adhesive in a procedure pack/tray that is to be sterilized prior to use. Exposure of DERMABOND adhesive, after its final manufacture, to excessive heat (as in autoclaves or ethylene oxide sterilization) or radiation (such as gamma or electron beam), is known to increase its viscosity and may render the product unusable.

PRECAUTIONS
- Do not apply liquid or ointment medications or other substances to the wound after closure with DERMABOND adhesive, as these substances can weaken the polymerized film and allow for wound dehiscence. DERMABOND adhesive permeability by topical medications has not been studied.
- DERMABOND adhesive permeability by fluids is not known and has not been studied.
- DERMABOND adhesive is a free flowing liquid slightly more viscous than water. To prevent inadvertent flow of liquid DERMABOND adhesive to unintended areas: (1) the wound should be held in a horizontal position, with DERMABOND adhesive applied from above, and (2) DERMABOND adhesive should be applied in multiple (at least 3), thin layers rather than in a few large droplets.
- Hold applicator away from yourself and the patient and break ampule close to its center one time only. Do not crush the contents of the applicator tube repeatedly as further manipulation of the applicator may cause glass shard penetration of the outer tube.
- DERMABOND adhesive should be used immediately after crushing the glass ampule as the liquid adhesive will not flow freely from the applicator tip after a few minutes.
- If unintended bonding of intact skin occurs, peel, but do not pull the skin apart. Petroleum jelly or acetone may help loosen the bond. Other agents such as water, saline, Betadine® Antibiotics, HIBICLENS† (chlorhexidene gluconate), or soap, are not expected to immediately loosen the bond.
- Safety and effectiveness of DERMABOND adhesive on wounds of patients with peripheral vascular disease, insulin dependent diabetes mellitus, blood clotting disorders, personal or family history of keloid formation or hypertrophy, or burst stellate lacerations, have not been studied.
- Safety and effectiveness of DERMABOND adhesive on the following wounds have not been studied: animal or human bites, puncture or stab wounds.
- Safety and effectiveness on wounds that have been treated with DERMABOND adhesive and then exposed for prolonged periods to direct sunlight or tanning lamps have not been studied.
- Safety and effectiveness of DERMABOND adhesive on wounds in vermilion surfaces has not been studied.

ADVERSE REACTIONS
- Adverse reactions encountered during clinical study:

Clinical Study Outcomes	*No Subcuticular Sutures*		*With Subcuticular Sutures*	
	DERMABOND	Control	DERMABOND	Control
	N (%)	N (%)	N (%)	N (%)
Accounting				
N, patients enrolled	240	243	167	168
N, patients treated	239	242	167	166
Patients completed	228 (95%)	215 (88%)	164 (98%)	162 (96%)
Adverse Reactions				
*Suspected Infection**	8 (3.6%)	2 (0.9%)	6 (3.6%)	2 (1.2%)
Wound type				
# Lacerations	8	2	1	0
# Incisions	0	0	5	2
Dehiscence with Need for Retreatment	6 (2.5%)	5 (2.1%)	3 (1.8%)	0
Acute Inflammation				
Erythema	26 (11.5%)	74 (33.0%)	52 (31.3%)	75 (45.1%)
Edema	22 (9.7%)	28 (12.5%)	62 (37.3%)	71 (42.8%)
Pain	14 (6.1%)	13 (5.8%)	56 (33.7%)	57 (34.3%)
Warmth	3 (1.3%)	6 (2.6%)	3 (1.8%)	4 (2.4%)

*In the clinical study, presence of infection was to be identified by observation of redness more than 3–5 mm from the repaired wound, swelling, purulent discharge, pain, increased skin temperature, fever, or other systemic signs of infection. (See clinical study). Confirmatory culture was not routinely obtained. Among cases of suspected infection for DERMABOND adhesive, 7/14 (50%) were in patients less than 12 years old with traumatic lacerations; overall, 8 of the 14 (approximately 60%) DERMABOND adhesive wounds with suspected infections were associated with sub-optimal cosmetic outcome.

- Reactions may occur in patients who are hypersensitive to cyanoacrylate or formaldehyde. See CONTRAINDICATIONS.
- The polymerization of DERMABOND adhesive on the skin releases small amounts of heat which may cause a sensation of heat or discomfort in some patients.
- Adverse reactions may be experienced following DERMABOND adhesive contact with the eye.

Manufactured for ETHICON, INC.
by Closure Medical Corp.
*Trademark

©Trademark of Purdue Fredericks
†Registered Trademark of Zeneca Pharmaceuticals

High Viscosity

DERMABOND*

Topical Skin Adhesive
(2-Octyl Cyanoacrylate)

INDICATIONS
High viscosity DERMABOND Topical Skin Adhesive is intended for topical application only to hold closed easily approximated skin edges of wounds from surgical incisions, including punctures from minimally invasive surgery, and simple, thoroughly cleansed, trauma-induced lacerations. High viscosity DERMABOND adhesive may be used in conjunction with, but not in place of, deep dermal stitches.

CONTRAINDICATIONS
- Do not use on any wound with evidence of active infection, gangrene, or wounds of decubitus etiology.
- Do not use on mucosal surfaces or across mucocutaneous junctions (e.g., oral cavity, lips), or on skin which may be regularly exposed to body fluids or with dense natural hair, (e.g., scalp).
- Do not use on patients with a known hypersensitivity to cyanoacrylate or formaldehyde.

WARNINGS
- High viscosity DERMABOND adhesive is a fast setting adhesive capable of adhering to most body tissue and many other materials, such as latex gloves and stainless steel. Inadvertent contact with any body tissue, and any surfaces or equipment that are not disposable or that cannot be readily cleaned with a solvent such as acetone should be avoided.
- Polymerization of high viscosity DERMABOND adhesive may be accelerated by water or fluids containing alcohol: High viscosity DERMABOND adhesive should not be applied to wet wounds.
- High viscosity DERMABOND adhesive should not be applied to the eye. If contact with the eye occurs, flush the eye copiously with saline or water. If residual adhesive remains, apply topical ophthalmic ointment to help loosen the bond and contact an ophthalmologist.
- When closing facial wounds near the eye with high viscosity DERMABOND adhesive, position the patient so that any run-off of adhesive is away from the eye. The eye should be closed and protected with gauze. Prophylactic placement of petroleum jelly around the eye, to act as a mechanical barrier or dam, can be effective in preventing inadvertent flow of adhesive into the eye. High viscosity DERMABOND adhesive will not adhere to skin pre-coated with petroleum jelly. Therefore, avoid using petroleum jelly on any skin area where high viscosity DERMABOND adhesive is intended to adhere. Use of DERMABOND adhesive near the eye has inadvertently caused some patient's eyelids to be sealed shut. In some of these cases, general anesthesia and surgical removal has been required to open the eyelid.
- High viscosity DERMABOND adhesive should not be used below the skin because the polymerized material is not absorbed by tissue and can elicit a foreign body reaction.
- High viscosity DERMABOND adhesive should not be used in high skin tension areas or across areas of increased skin tension, such as knuckles, elbows, or knees, unless the joint will be immobilized during the skin healing period.
- High viscosity DERMABOND adhesive treated wounds should be monitored for signs of infection. Wounds with signs of infection, such as erythema, edema, warmth, pain and pus, should be evaluated and treated according to standard practice for infection.
- High viscosity DERMABOND adhesive should not be used on wound sites that will be subjected to repeated or prolonged moisture or friction.
- High viscosity DERMABOND adhesive should only be used after wounds have been cleaned, debrided and are otherwise closed in accordance with standard surgical practice. Local anesthetic should be used when necessary to assure adequate cleansing and debridement.
- Excessive pressure of the applicator tip against wound edges or surrounding skin can force the wound edges apart and allow adhesive into the wound. Adhesive within the wound could delay wound healing and/or result in adverse cosmetic outcome. Therefore, high viscosity DERMABOND adhesive should be applied with a very light brushing motion of the applicator tip over easily approximated wound edges.
- High viscosity DERMABOND adhesive polymerizes through an exothermic reaction in which a small amount of heat is released. With the proper technique of applying high viscosity DERMABOND adhesive in multiple thin layers (at least three) onto a dry wound and allowing time for polymerization between applications, heat is released slowly and the sensation of heat or pain experienced by the patient is minimized. However, if high viscosity DERMABOND adhesive is applied so that large droplets of liquid are allowed to remain unspread, the patient may experience a sensation of heat or discomfort.
- High viscosity DERMABOND adhesive is packaged for single patient use. Discard remaining opened material after each wound closure procedure.
- Do not resterilize high viscosity DERMABOND adhesive.
- Do not place high viscosity DERMABOND adhesive in a procedure pack/tray that is to be sterilized prior to use. Exposure of high viscosity DERMABOND adhesive, after its final manufacture, to excessive heat (as in autoclaves or ethylene oxide sterilization) or radiation (such as gamma or electron beam), is known to increase its viscosity and may render the product unusable.

PRECAUTIONS
- High viscosity DERMABOND adhesive has not been evaluated for use on wounds such as surgical incisions, punctures from minimally invasive surgery.
- Do not apply liquid or ointment medications or other substances to the wound after closure with high viscosity DERMABOND adhesive, as these substances can weaken the polymerized film and allow for wound dehiscence. High viscosity DERMABOND adhesive permeability by topical medications has not been studied.
- High viscosity DERMABOND adhesive permeability by fluids is not known and has not been studied.
- High viscosity DERMABOND adhesive, as a liquid, is syrup-like in viscosity. To prevent inadvertent flow of liquid high viscosity DERMABOND adhesive to unintended areas: (1) the wound should be held in a horizontal position, with high viscosity DERMABOND adhesive applied from above, and (2) high viscosity DERMABOND adhesive should be applied in multiple (at least 3), thin layers rather than in a few large droplets.
- Hold applicator away from yourself and the patient and break ampule close to its center one time only. Do not crush the contents of the applicator tube repeatedly as further manipulation of the applicator may cause glass shard penetration of the outer tube.
- High viscosity DERMABOND adhesive should be used immediately after crushing the glass ampule as the liquid adhesive will not flow freely from the applicator tip after a few minutes.
- If unintended bonding of intact skin occurs, peel, but do not pull the skin apart. Petroleum jelly or acetone may help loosen the bond. Other agents such as water, saline, Betadine® Antibiotics, HIBICLENS† (chlorhexidene gluconate), or soap, are not expected to immediately loosen the bond.
- Safety and effectiveness of high viscosity DERMABOND adhesive on wounds of patients with peripheral vascular disease, insulin dependent diabetes mellitus, blood clotting disorders, personal or family history of keloid formation or hypertrophy, or burst stellate lacerations, have not been studied.
- Safety and effectiveness of high viscosity DERMABOND adhesive on the following wounds have not been studied: animal or human bites, puncture or stab wounds.
- Safety and effectiveness on wounds that have been treated with high viscosity DERMABOND adhesive and then exposed for prolonged periods to direct sunlight or tanning lamps have not been studied.
- Safety and effectiveness of high viscosity DERMABOND adhesive on wounds in vermilion surfaces has not been studied.

ADVERSE REACTIONS
Adverse reactions encountered during the clinical study for closure of trauma-induced lacerations using high viscosity DERMABOND adhesive and the clinical study comparing low viscosity DERMABOND adhesive to sutures, staples, and adhesive strips are listed below:

The safety of both high viscosity DERMABOND adhesive and the low viscosity DERMABOND adhesive control was measured in a randomized clinical study of 84 patients, 42 patients receiving high viscosity product and 42 receiving low viscosity product, by 1) the presence or the extent of an inflammatory reaction, 2) the presence of signs of clinical infection, 3) cosmetic outcome at Day 30, 4) assessment of thermal discomfort, and 5) the reported adverse events associated with use of the device. No significant differences between the two treatment groups were observed for any of these safety outcome measures, although 17 patients (44%) randomized to the high viscosity DERMABOND adhesive treatment group experienced a sensation of heat during application of the skin adhesive compared to 10 patients (26%) randomized to the low viscosity DERMABOND adhesive treatment group. Of those 17 patients in the high viscosity group, 5 of the patients noted that sensation of heat was uncomfortable. None of the patients in the low viscosity group observed objectionable sensation of heat.

As indicated under WARNINGS, high viscosity DERMABOND adhesive polymerizes through an exothermic reaction in which heat is released. It is important to use the proper technique of applying high viscosity DERMABOND adhesive in thin layers to minimize the risk that the patient may experience a sensation of heat or discomfort. This is especially important in the application of high viscosity DERMABOND adhesive, because the increased viscosity of the product relative to low viscosity DERMABOND adhesive can create a thicker applied layer resulting in a higher potential for heat to be generated. High viscosity DERMABOND adhesive should always be applied in thin layers so that large amounts of liquid are not allowed to collect, resulting in thermal discomfort for the patient.

Adverse reactions encountered during clinical study comparing low viscosity DERMABOND adhesive to sutures, staples, and adhesive strips are listed in the table to the left.

- Reactions may occur in patients who are hypersensitive to cyanoacrylate or formaldehyde. See CONTRAINDICATIONS.
- Adverse reactions may be experienced following high viscosity DERMABOND adhesive contact with the eye.

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DERMABOND® Topical Skin Adhesive . . . An Advantage in the ED

- Offers ease of use for a variety of wounds
- Is the first and only FDA-approved topical skin adhesive that protects wounds from bacteria that can lead to infection
- Provides the strength of healed tissue at 7 days in less than 3 minutes[2]
- Is more cost-effective than sutures[3-6]
- Comes in a choice of formulations: original and high viscosity

DERMABOND* Topical Skin Adhesive 2-Octyl Cyanoacrylate	Product Code	Size	Packaging
High Viscosity	DHV12	0.5 mL	12 Applicators per Box
High Viscosity With Precision Tip	HVN6	0.5 mL	6 Applicators per Box
Original	DB12	0.5 mL	12 Applicators per Box
Original With Chisel Tip	DBC12	0.5 mL	12 Applicators per Box

For more information, call the ETHICON Clinical Call Center at **1-877-384-4266, Option 1.**

For training tips and a CME opportunity, visit **www.dermabondtraining.com.**

†*Enterococcus faecium, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Staphylococcus epidermidis*

References: 1. McCaig LF and Burt CW. *National Hospital Ambulatory Medical Care Survey: 1999.* Advance data from vital and health statistics; no. 320. Hyattsville, Md: National Center for Health Statistics. 2001. 2. Data on file, ETHICON, INC. 3. Quinn J et al. A randomized trial comparing octylcyanoacrylate tissue adhesive and sutures in the management of lacerations. *JAMA.* 1997;227(19):1527-1530. 4. Bruns TB et al. A new tissue adhesive for laceration repair in children. *J Pediatr.* 1998;132(6):1067-1070. 5. Theodore N et al. *The Economics of DERMABOND in Neurosurgical Wound Closure.* Phoenix, Ariz: Neuroscience Publications, Barrow Neurological Institute, March 2001:2-10. 6. Osmond MH et al. Economic comparison of a tissue adhesive and suturing in the repair of pediatric facial lacerations. *J Pediatr.* 1995;126:892-895.

Technique tips should not be considered a substitution for the DERMABOND Topical Skin Adhesive Instructions for Use.

Original DERMABOND Adhesive With Dome and Chisel Tip Applicators

High Viscosity DERMABOND Adhesive With Dome and Precision Tip Applicators

DERMABOND*
TOPICAL SKIN ADHESIVE
2-Octyl Cyanoacrylate

Advances in healing

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